

72  
S1

What is claimed is:

1. A recombinant adenovirus expression vector comprising a partial or total deletion of a protein IX DNA and a gene encoding a foreign protein.
2. The recombinant adenovirus expression vector of claim 1, wherein the deletion of the protein IX gene sequence extends from about 3500 bp from the 5' viral termini to about 4000 bp from the 5' viral termini.
3. The recombinant adenovirus expression vector of claim 2 further comprising deletion of a non-essential DNA sequence in adenovirus early region 3 and/or early region 4.
4. The recombinant adenovirus expression vector of claim 2 further comprising deletion of a DNA sequences designated adenovirus E1a and E1b.
5. The recombinant adenovirus expression vector of claim 2 further comprising deletion of early region 3 and/or 4 and DNA sequences designated adenovirus E1a and E1b.
6. The recombinant adenovirus expression vector of claim 4 or 5 further comprising a deletion of up to forty nucleotides positioned 3' to the E1a and E1b and protein IX deletion and a foreign DNA molecule encoding a polyadenylation signal.
7. The recombinant adenovirus expression vector of claims 1 to 6, wherein the adenovirus is a Group C adenovirus selected from a serotype 1, 2, 5 or 6.

2020 RELEASE UNDER E.O. 14176

73  
62

8. The recombinant adenovirus expression vector of claim 1, wherein the gene is a DNA molecule up to 2.6 kilobases.

9. The recombinant adenovirus expression vector of claim 6, wherein the gene is a DNA molecule up to 4.5 kilobases.

10. The recombinant adenovirus expression vector of claim 1, wherein the gene encodes a foreign functional protein or a biologically active fragment thereof.

11. The recombinant adenovirus expression vector of claim 10, wherein the gene encodes a foreign functional tumor suppressor protein or a biologically active fragment thereof.

12. The recombinant adenovirus expression vector of claim 1, wherein the gene encodes a suicide protein or functional equivalent thereof.

13. A transformed host cell comprising the recombinant adenovirus expression vector of claim 1 or 10.

14. The transformed host cell of claim 13, wherein the host cell is a prokaryotic or eucaryotic cell.

15. A method for transforming a pathologic hyperproliferative mammalian cell comprising contacting the cell with the expression vector of claim 1.

16. A method of treating a pathology in an animal or mammal caused by the absence of a tumor suppressor gene or the presence of a pathologically mutated tumor suppressor gene comprising administering to the animal or mammal an effective amount of the vector of claim 1 containing a gene encoding a foreign functional protein

SEARCHED - INDEXED - SERIALIZED - FILED

SUB B!  
CONT'D.

74  
63

*Sub B*  
*CONCL'D.*

having a tumor suppressive function, under suitable conditions.

17. The method of claim 16, wherein the foreign protein is a functional tumor suppressor protein.

*Sub B2*

18. A method of gene therapy comprising administering to a subject an effective amount of the vector of claim 1.

19. A method of inhibiting the proliferation of a tumor in an animal comprising administering an effective amount of the adenoviral expression vector of claim 1 under suitable conditions to the animal.

20. The method of claim 19, wherein the gene encodes an anti-tumor agent.

21. The method of claim 20, wherein the anti-tumor agent is a tumor suppressor gene.

22. The method of claim 20, wherein the anti-tumor agent is a suicide gene or functional equivalent thereof.

*Sally C5*

23. The method of claim 21, wherein the tumor is non-small cell lung cancer, small cell lung cancer, hepatocarcinoma, melanoma, retinoblastoma, breast tumor, colorectal carcinoma, leukemia, lymphoma, brain tumor, cervical carcinoma, sarcoma, prostate tumor, bladder tumor, tumor of the reticuloendothelial tissues, Wilm's tumor, astrocytoma, glioblastoma, neuroblastoma, ovarian carcinoma, osteosarcoma, and renal cancer.

24. The method of claim 19, wherein the vector is administered by intra-tumoral injection.

75  
64

25. A pharmaceutical composition comprising the recombinant adenoviral expression vector of claim 1, 10 or 12.

*Sub B3*

26. A method for reducing the proliferation of tumor cells in a subject comprising administering under suitable conditions an effective amount of an adenoviral expression vector of claim 12 and an effective amount of a thymidine kinase metabolite or a functional equivalent thereof.

27. The method of claim 26, wherein the thymidine kinase metabolite is ganciclovir or 6-methoxypurine arabinonucleoside or a functional equivalent thereof.

28. The method of claim 26, wherein the adenoviral expression vector is administered by injection into the tumor mass.

29. The method of claim 26, wherein the tumor cells are hepatocellular carcinoma.

30. The method of claim 29, wherein the adenoviral expression vector is administered directly into the hepatic artery of the subject.

B

31. A kit for reducing the proliferation of tumor cells comprising the components of the adenoviral expression vector of claim 12, a thymidine kinase metabolite or functional equivalent thereof, pharmaceutical carriers and instructions for the treatment of hepatocellular carcinoma using the kit components.

Add  
C2